## REMARKS

Claims 1-11 and 13-14, 18-25 and 32-51 are currently pending. Claim 12 was cancelled in the amendment submitted June 2, 2003. Claims 15-17, 26-1 and 52-58 have been cancelled. Claims 1, 3-4, 25, 32, 34-35 and 49 have been amended. Support for the amendment recited in these claims is seen on page 3, lines 10-19 of the specification. The claims have been amended to explicitly state what was implicit in the original claims. Accordingly, such amendments do not operate to narrow the claims in any way and are not intended to act as an estoppel in any way. Any modification and variation may be made in the claims herein described are made without departing from the spirit and scope of the present invention. The scope of the present invention is defined by the claims, which includes known equivalents and unforeseeable equivalents at the time of filing of this application.

Interview Summary:

A telephonic interview was conducted with Examiner Azpuru on January 27, 2005. During that interview, the Examiner and Applicants representative, Andrea Small, discussed the rejections set forth in office action mailed 12/03/2004. The following determinations were made:

(a) The office action of 12/03/2004 is a non-final action;

(b) The double patenting rejection outlined on page 8 of the office action is made in view of application number 10/729,543 and not 09/729,543;

(c) Specific amendment options were discussed, which if made, the Examiner indicated would place the application in condition of allowance; and

(d) The examiner indicated that providing a duplicate of the declaration under 37 CFR 1.132, provided with response filed August 18, 2004, with this response is unnecessary.

The Applicants would like to thank the Examiner for his courteous manner and helpful suggestions offered during the interview.

Rejection under 35 USC 103(a):

Claims 1-11, 13, 14, 18-25 and 32-51 are rejected as being unpatentable over Arnold, et al in view of Ahmed.

The Examiner states that Arnold discloses an inhalable powder which combines finer and coarser particles. The Examiner contends that "Arnold et al clearly discloses the type of

inhalable powder and method of manufacturing it, as well as the inclusion of bioactives." Additionally, that even though Arnold does not teach the inclusion of tiotropium as the inhalable bioactive or its use in the treatment of COPD and specifically asthma, the Ahmed reference compensates for this lack of teaching and provides the necessary suggestion and/or motivation to modify the teachings of Arnold by the fact that Ahmed discloses medications such as tiotropium bromide and are specifically recited for this therapeutic use at col. 6, line 57. Applicants respectfully traverse.

The Examiner has failed to establish a prima facie case of obviousness. The objective of the instant invention to provide for tiotropium containing powders that, while being administered via inhalation lead to a high inhalable fraction of the active ingredient and a low variability of the said inhalable fraction (see introductory part of the specification) in a batch to batch comparison.

This low variability between different batches is of particular importance if the active ingredient is that efficient that it is present in only small amounts (a high variability from batch to batch would not allow to administer the prescribed amount of active ingredient in a reproducable manner).

The invention at hand proposes as a solution to this problem the mixture of tiotropium with an excipient mix containing a specific amount of finer excipent (e.g. lactose 5μm) to coarser excipient (e.g. lactose of larger particle size).

Arnold et al. disclose that the inhalable fraction of an active ingredient can be enhanced if finer excipient is added to coarser excipient. The examples according to Arnold et al show that the larger the amount of finer excipient the larger the inhalable fraction.

However, Arnold is silent with respect to the "variability" issue. A person of ordinary skill in the art would have concluded from Arnold et al that it is best to have as much fine excipient present as conceivable. This clearly teaches away from the instantly claimed invention.

Also, Arnold fails to teach specific limitations of the instant claims which include the percent amount of active ingredient based on the formulation as a whole required in the instant

claims, which is in the range of 0.4 to 0.8%, whereas Arnold teaches a percent amount of active ingredient based on the amount of excipient used, which is 0.2%, the amount of active ingredient used based on the formulation as a whole in the Arnold reference is seen in Example 1 and 2 in the tables in column 2 (14.4%-38.3%). These ranges are clearly outside of the ranges required by the instant claims. Thus, Arnold clearly does not teach the specific limitations of the instant claims.

The Ahmed reference does not provide any teaching or suggestion to modify the tiotropium bromide disclosed therein could be prepared in the manner as instantly claimed.

Therefore, it is the Applicants contention that the Arnold and Ahmed references either alone or in combination do not teach or fairly suggest the instantly claimed invention.

However, assuming arguendo that the Examiner has in fact established a prima facie case of obviousness, a declaration, filed under 37 CFR 1.132, filed with response of August 18, 2004, provides the necessary comparison which shows experimental results obtained for the tiotropium containing powder mixtures according to the instant invention show that these powder mixtures allow the inhalable proportion of active substance tiotropium to be administered with the lowest possible variability. Furthermore, the superiority of the instant powder mixtures is not taught, suggested, or deducible by the cited prior art. Moreover, these findings would have been both surprising and unexpected to one of ordinary skill in the art at the time the invention was made.
It was determined that there is a certain batch to batch variability given, if the inhalable fraction of tiotropium is measured for powder mixtures containing no fine excipient.

It was found that this variability decreases if 5% of fine excipient are added (= formulation samples according to example 2 of the invention).

The most important aspect, however, is that this decrease in batch to batch variabilty is not observed if in line with Arnold's suggestion, i.e. increasing the amount of fine excipient is further increased. The variability increases when 10% of fine lactose are added (= formulation samples according to example 3 of the invention). Counter intuitively, it was observed that the variability of these mixtures increases when the mixtures are without finer

excipients. The fact that only a specific amount (as specified in claim 1) reduces the variability is surprising and by no way deducible from Arnold et al.

Neither the other references are able to lead the person of ordinary skill in the art to this finding. Even more, it has to be observed that all references are totally silent with respect to the problem of an uncontrolled batch to batch variability.

Thus, withdrawal of the rejection is respectfully requested.

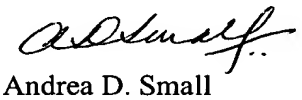
Double Patenting:

Claims 1-11 and 18-57 have been rejected as being provisionally rejected under 35 USC 101 as claiming the same invention as that of claims 1-11 and 17-58 of Application No. 10/729,543. Applicants would like to point out that application no. 10/729,543 has been abandoned, therefore, the aforementioned rejection is moot. Withdrawal of the rejection is respectfully requested.

In view of the above remarks, Applicants respectfully submit that this application is now in condition for allowance and earnestly request such action.

If any points remain at issue which can best be resolved by way of a telephonic or personal interview, the Examiner is kindly requested to contact the undersigned attorney at the telephone number listed below.

Respectfully submitted,



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